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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Philip S Johnson
Jonhson & Jonhson
One Jonhson & Jonhson Plaza
New Brunswick, NJ 08933-7003

EXAMINER	
AKHAVAN, RAMIN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,011	CONTRERAS,	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6-9,15-17 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4* is/are allowed.

6)☒ Claim(s) *1,2,6-9,15-17 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a response, filed 09/19/2005, amending claims 1-2, 4 and 6-9. Claims 1-17, 22-26, 28-35, 38-48 are pending in this Application. Claims 3, 5, 10-14, 22-26, 28-34 and 38-48 were withdrawn from consideration as drawn to nonelected subject matter for reasons of record. Thus, claims 1-2, 4, 6-9, 15-17 and 35 are currently pending and under consideration in this action.

All objections/rejections not repeated herein are hereby withdrawn. Where applicable, a response to Applicant's arguments will be set forth immediately following the body of any objections/rejections repeated herein. As new grounds of rejection are set forth herein, this action is non-final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Claims 1-2, 6-9, 15-17 and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.**

This rejection is new insofar as claims 15-17 and 35 are rejected. Said claims are directed to embodiments that encompass the genus of nucleic acids of base claim 1, but the claims were inadvertently omitted from the rejection in the action mailed 06/16/2005. Furthermore, the rejection herein below is modified to address material change to independent claim 1, i.e., replacing 70% homology with 90% homology.

The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. More particularly, the claims are directed to a genus of nucleic acid molecules, wherein said genus is comprised of a subgenus of nucleic acid molecules having at least 90% homology to SEQ ID NO: 1, or a subgenus of nucleic acid molecules that are a "fragment or derivative" of SEQ ID NO: 1. Thus as written, the claimed nucleic acid molecule can have the requisite homology over any span of sequences within SEQ ID NO: 1 (i.e., the claim does not read on homology "over the full length of" SEQ ID NO: 1). Said nucleic acid molecules (i.e., structures) must correlate to a function of encoding a polypeptide that is "critical for survival and growth of the yeast Candida albicans". Given the size of SEQ ID NO: 1, even where limited to nucleic acid molecules that are 90% homologous the genus comprises tens of thousands of potential nucleic acid molecules. Further, the subgenus of "a fragment or derivative" is comparable in size, given that the subgenus encompass fragments or derivatives of any undefined size and composition (e.g., the term "derivative" reads on nucleotide substitutions, deletions or insertions).

The written description requirement for a claimed genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure or by a combination of such identifying characteristics sufficient to show applicant was in possession of the claimed genus.

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. *Lockwood v. American Airlines Inc.* (CAFC) 41 USPQ2d 1961 (at 1966). Further, the Guidelines for Written Description state:

> "The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art" (Federal Register/ Vol. 66, No. 4/Friday, January 5, 2001/Notices, column 1, page 1105). "[t]he claim as a whole, including all limitations found in the preamble, the transitional phrase, and the body of the claim, must be sufficiently supported to satisfy the written description requirement" (at page 1105, center column, third full paragraph).

The critical feature in the instant claims is the nucleic acid structure as claimed and having the prescribed function of encoding a critical protein. Therefore, in the context of the instant claims, a sufficient description would identify a representative number of nucleic acid molecules that are at least 90% homologous to SEQ ID NO: 1, or that are fragments or derivatives of SEQ ID NO: 1, and correlate to function of encoding a protein that is itself critical for *C. albican* survival and growth. The specification does not identify a representative number of embodiments comprised in the genus/subgenus of claimed nucleic acid molecules.

The specification discloses that SEQ ID NO: 1 encodes the protein SAM2 (e.g., Specification, p. 35), but there is no further clarification of particular domains, motifs, sequences, or any other structural feature, that can be identified as a necessary sequence that encodes a necessary portion of a protein that is critical for both survival and growth. No regions are disclosed that are at least 90% homologous to SEQ ID NO: 1 or that are fragments or derivatives thereof and that maintain the function of encoding a critical polypeptide or domains thereof.

Moreover, there are no biochemical or functional assays to confirm whether SEQ ID NO: 1 actually encodes a SAM2. Rather, the prescribed enzyme (i.e., SAM2) is ascribed to an isolated gene fragment, which shares 74% identity with *S. cerevisiae* SAM2 gene. (Id.). The gene fragment is subsequently utilized to identify clone 36.13.1, which contains the complete open reading frame of the purported SAM2 gene including flanking regions. (p. 36, middle). Thus if it is unknown whether the full-length gene encodes a functional protein (i.e., SAM2) it is reasonable to conclude that a given fragment or derivative or any sequence having 90% homology over any region of the full-length gene (including flanking regions) – all within the claimed genus and subgenus – would also be unpredictable insofar as a given structure must correspond with the requisite functionality of encoding a polypeptide that inheres an activity necessary for growth and survival.

As such, there is a gap in the disclosure with respect to identities of species that comprise the genus/subgenus of nucleic acid molecules that are claimed but that must correspond to the requisite function (e.g., 90% homologous or any fragment of SEQ ID NO: 1 and that are critical for growth and survival). Furthermore, this gap is not filled by knowledge available in the art. In other words, the art does not provide clarification of sequences that are 90% homologous to SEQ ID NO: 1, that are fragments or derivative of SEQ ID NO: 1 and that encode a critical protein or at least a critical portion of the protein that are necessary for *C. albican* growth and survival.

Given the enormous breadth of the nucleic acid molecules encompassed by the rejected claims, and given the limited description from the instant specification of such nucleic acid molecules, the skilled artisan would not have been able to envision a sufficient number of

specific embodiments to describe the broadly claimed genus/subgenus. Moreover, an applicant claiming a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from other species. Therefore, the skilled artisan would reasonably have concluded that applicants were not in possession of the claimed invention.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant's only assertion is that Applicants are entitled to claim variants of the claimed sequence that are expected to encode a protein having the recited activity. (Remarks, p. 11, ¶¶ 3-4). No other factual or scientific reasoning is provided.

At the outset, as written the claimed genus and subgenus are directed to nucleic acids that encode a protein that encodes some undefined activity that is critical for survival and growth. Thus, it is unclear to what specific protein activity Applicants are referring. However, if Applicant is implying that that the protein has the activity of a SAM2, i.e., methionine S-adenosyl transferase, such a limitation is not claimed. Irrespective, there is no substantive evidence provided to show that SEQ ID NO: 1 encodes a protein having SAM2 activity. Indeed, as noted above, SAM2 is selected based on a 600 base pair fragment having about 70% identity to a *S. cerevisiae* SAM2 gene. (Specification, p. 35, last ¶).

One of skill will readily recognize that identification of a specific protein activity merely on percent homology, and especially where a gene fragment is utilized as a probe, is not predictive of protein functionality. Put another way structure to function correlations cannot be predicted based on homology analysis alone, one of ordinary skill in the art would have a

legitimate basis to doubt the credibility of the asserted specific and substantial utilities for the isolated polynucleotides of the invention. As evidence in the art suggests, to attempt to predict activity based on homology is unpredictable at best.

For example, the relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable as evidenced by Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). Berendsen explicitly states that "one of the 'grand challenges' of high-performance computers – predicting the structure of proteins – acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain." (p. 643, ¶ 4). The reference further teaches about the unpredictability in the art concerning protein structure, and failures to make it predictable in regard to function. Thus, as evidenced by knowledge in the art, it is likely that an envisioned nucleic acid sequence, fragment or derivative that is 90% homologous as compared to SEQ ID NO: 1 would not necessarily encode a protein or protein fragment that encodes an activity that is necessary for growth and survival, assuming the resulting polypeptide encodes an activity at all.

Thus the relevant art teaches, to attempt to predict activity based on homology is unpredictable at best. (Supra, Berendsen, 1998, at p. 2; indicating that accurate prediction of activity cannot be based on primary structure alone). Furthermore, one of skill would recognize that it is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences, which is further complicated by the modular nature of many proteins. (See, Attwood. Science. 2000; 290:471-3; p. 472, col. 2). Additional factors that also complicate functional assignment include: redundancy, nonorthologous displacement replacing

genes with unrelated but functionally analogous genes, horizontal gene transfer introducing gene from different phylogeneic lineages and lineage-specific gene loss eliminating ancestral genes. (Id.). Moreover, assessing the actual power of the context based method for protein function prediction, such as that based on homology, requires extensive testing by labor-consuming, case-by-case experimental analysis. (See, Galperin et al. 2000. Nat. Biotech; 18:609-13). In sum, the disclosure lacks sufficient description to support the claimed genus and subgenus of nucleic acids that must encode proteins that encode some undefined function, where said function is necessary for *C. albicans*' survival and growth.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. **Claims 1-2, 6-9, 15-17 and 35 are rejected under 35 U.S.C. 102(e) as being anticipated by Weinstock et al. (US 6,747,137; see entire document; hereinafter '137 patent).**

This rejection is new insofar as the rejection of record is modified to address material changes to claim 1, and the claims' interpretation is clarified in regard to the breadth of the limitation "homologous to SEQ ID NO: 1".

The claims are directed to nucleic acid molecules that most particularly comprise a fragment having at least 90% homology *to any span or region* of SEQ ID NO: 1 or having from 10 to 50 contiguous nucleic acid sequences of *any span or region* of SEQ ID NO: 1. In addition, claims are directed to expression vectors comprising nucleic acid molecules comprising at sequences that are at least 90% homologous to SEQ ID NO: 1.

The '137 patent teaches the nucleic acid molecule of SEQ ID NO: 5972, which is 81% homologous *over the entire length* of SEQ ID NO: 1. (e.g., col. 1272; col. 7, ll. 35-45; col. 8, ll. 5-20; col. 26). However, within the span or regions of SEQ ID NO: 1, there are portions that are at least 90% identical (e.g., 100% identity) to portions or regions of SEQ ID NO: 1. In other words, as written the limitation homologous is not relative to the entire length of SEQ ID NO: 1. Furthermore, within the regions of identity (i.e., sequences encompassed by SEQ ID NO: 5972), there are contiguous stretches of 10-50 nucleotides that meet the claimed limitations of claim 35.

In addition, the nucleic acid molecules disclosed can be further comprised in expression vectors (e.g., col. 8, ll. 25-40), which include inducible promoters (e.g., col. 14, last ¶, bridging to col. 15; col. 20, ll. 1-65, bridging to col. 21; col. 25, ll. 25-55). In addition, the vectors can contain a reporter gene (i.e., selectable markers). (e.g., col. 20, last ¶). In sum, the '137 teaches all the limitations of the rejected claims.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant asserts since SEQ ID NO: 5972 is not at least 90% over SEQ ID NO: 1, then it cannot anticipate the rejected claims. As noted above, independent claim 1 does not read on "homologous over the full length of SEQ ID NO: 1".

It would be remedial to amend the claim to indicate that homology is over the full-length of SEQ ID NO: 1. However, if such an amendment were made, claims 9 and 35 would still be anticipated. First, as to claim 9, the limitation "high stringency conditions" is not exclusively defined in the specification. As such, a broad reasonable interpretation of said limitation would include sequences that are less than 90% homologous over the entire length of SEQ ID NO: 1 (e.g., 80%), but that would hybridize to SEQ ID NO: 1 under the reasonable and broad interpretation of the limitation "high stringency". In addition, claim 9 is directed to any molecule that hybridizes to the nucleic acid molecules encompassed by claim 1. In other words, claim 9 encompasses molecules that do not necessarily have to be 90% homologous to SEQ ID NO: 1, but merely are required to hybridize to molecules under the broad limitation of "high stringency".

Second, regarding claim 35, any sequence comprising 10 to 50 contiguous nucleotides as compared to any portion of SEQ ID NO: 1 anticipates the claim. Thus, the '137 patent discloses a sequence that comprises the necessary structural limitations recited in claim 35, irrespective of whether the nucleic acids of the base claim are homologous over a portion or the entire length of SEQ ID NO: 1. In sum, as written, the '137 patent anticipates the rejected claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. **Claims 1-3, 6-9, 15-17 and 35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-21 and 23-28 of copending Application No. 10/451,467.**

This rejection is new insofar the rejection of record is modified to further clarify the breadth of the claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. Although the conflicting claims are not identical, they are not patentably distinct from each other because while the claims do not recite the same exact limitations, they are directed to indistinguishable subject matter.

The instant and reference claims are directed to nucleic acid molecules and expression vectors comprising said nucleic acid molecules, which are delimited to instant SEQ ID NO: 1 and reference SEQ ID NOs: 475, 579 and 687, each of which is at least 88.9% homologous to at least certain portions of SEQ ID NO: 1. Therefore, the instant claims are obvious over the reference claims.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. In view of the breadth of the claims as discussed above, that the base claim 1 is amended to recite "90%" homology does not obviate this rejection, because the claimed sequences are not delimited to homology over the entire length of SEQ ID NO: 1.

In addition, as stated above, if sequence homology were over the entire length of SEQ ID NO: 1 would not distinguish the nucleic acid molecules of claim 9 and 35. (Supra, Rejection No. 2, Response to Arguments).

Conclusion

Claim 4 is allowed. Claims 1-2, 6-9, 15-17 and 35 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached between 8:30-5:00, Monday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD, can be reached on 571-272-0781. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully submitted,

Ray Akhavan/AU 1636

DANIEL M. SULLIVAN
PATENT EXAMINER